REMARKS

Status of the Claims.

Claims 1-21 are pending with entry of this amendment, no claims being cancelled and no claims being added herein. Claim 1 is amended herein. This amendment introduces no new matter. Support is replete throughout the specification (*see, e.g.*, 9, lines 5-7, page 11, lines 1-11, page 3, lines 17-18, and so forth). It is noted that the amendments made herein, do not alter the scope of the claimed invention and are made for clarity not for purposes of patentability.

35 U.S.C. §102.

The rejection of claims 1, 3-8, and 10-18 under 102 (e) as allegedly anticipated by Anderson *et al.* (U.S. Patent No: 6,168,948 B1) was maintained. In particular, the Examiner that the features relied upon by Applicants ("different binding partners", "different analytes", and spatial segregation of different analytes") are not recited in the claims. Applicants traverse by argument and amendment.

The Examiner is respectfully reminded that anticipation requires that "**all limitations** of the claim are found in the reference, or 'fully met' by it." [emphasis added] *Kalman v Kimberly-Clark Corp.*, 218 USPQ 781, 789 (Fed. Cir. 1983).

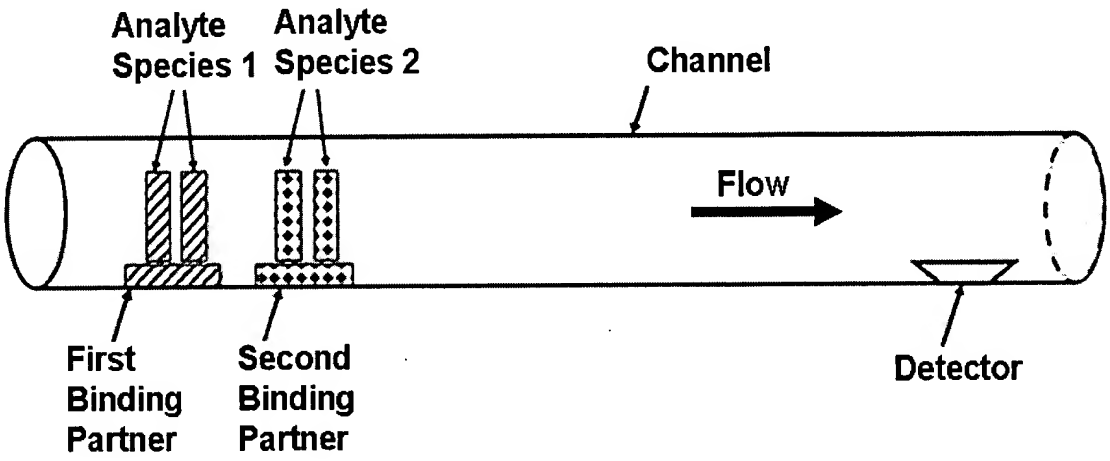
Claim 1, as amended herein recites:

> Claim 1. (Currently Amended): A method of detecting two or more target analytes in a sample, said method comprising:
>
> i) providing a channel having affixed therein **a first binding partner specific for a first analyte and a second binding partner specific for a second analyte, wherein said first binding partner and said second binding partner are specific for different analytes**, and **said first binding partner and said second binding partner are located in different regions of said channel** and said channel has a cross-sectional area small enough such that when analytes are released from said first binding partner and said second binding partner into a fluid flowing through said channel, said analytes remain spatially segregated until they reach a detection point in said channel downstream from said binding partners;
>
> ii) passing a fluid comprising said sample through said channel under conditions where said target analytes present in said sample bind to their respective binding partners thereby spatially encoding said analytes in said channel;
>
> iii) releasing said analytes from the binding partners into said fluid

passing along said channel **whereby said analytes are spatially segregated**; and

iv) detecting said analytes at a position in said channel downstream from the binding partners.

One embodiment of this invention showing multiple analytes (analyte species 1, 2) is illustrated schematically below:



Anderson *et al.* **fails to disclose** or to even suggest method utilizing a device comprising a channel having affixed therein **a first binding partner specific for a first analyte and a second binding partner specific for a second analyte, where the first binding partner and the second binding partner are specific for different analytes**, where the **first binding partner and the second binding partner are located in different regions of the channel.**

In contrast, the device disclosed by Anderson *et al.* contains at most **a single species of binding partner** and is **incapable of spatially segregating analytes** along a channel as is accomplished in the presently claimed device. Thus, for Example, the embodiment identified by the Examiner contains only a single species of binding partner (a poly-T oligonucleotide):

> In another embodiment of the present invention, a miniaturized m-RNA purification system and method are disclosed. Since messenger RNA comprises only a small fraction (e.g., about 20%) of the total cell RNA, it would be desirable to purify m-RNA from messenger expression monitoring applications. Messenger RNA can be distinguished by its poly-A tail. **In this device, poly-T oligos are tethered on a high surface geometry**. The messenger RNA will selectively hybridize to these oligonucleotides.

> Referring to FIG. 27, a messenger RNA purification system 2900 includes a sheet 2902, such as polycarbonate, glass, silicon, or polypropelene, polystyrene, polyethylene, acrylic, and commercial polymers, and a substrate 2904 (e.g., silicon) having a plurality of ridges 2906 between the sheet 2902 and substrate 2904. Preferably, sheet 2902 is a polymer and substrate 2904 is silicon, but such composition is not limiting as other workable compositions are equally possible. The ridges 2906 are preferably formed using reactive ion etching or other conventional techniques. **Poly T oligos or other affinity treatment 2912 are attached to ridges 2906, as discussed below**. A piezoelectric crystal 2908 is preferably mounted to the polymeric sheet 2902 opposite substrate 2904. [emphasis added] (col. 41, lines 22-44)

This embodiment comprises only a single species of binding partner; poly-T oligos (oligonucleotides). Moreover, that single species of binding partner appears to be distributed throughout the reaction chamber (*see, e.g.,* 2912 in Figure 27 and accompanying explanation).

All species of mRNAs in the sample will bind to the poly-T oligos by virtue of their complementary poly-A tails. Because there is only a single species of binding partner (poly-T oligos), and all the mRNAs have poly-A tails, hybridization will result in the distribution of various mRNAs throughout the chamber **2910. No spatial segregation of different analytes (different mRNAs) can occur.**

Even if the Examiner regards the mRNA as a first analyte, and the remaining RNA as a second analyte, the device disclosed by Anderson *et al.* fails to anticipate the presently pending claims. Anderson *et al.* discloses only a single binding partner (poly-T oligos). There is no binding partner for the RNA that is not mRNA.

In summary, Anderson *et al.* :

1) Fails to disclose a device comprising a channel having affixed therein **a first binding partner specific for a first analyte and a second binding partner specific for a second analyte, wherein said first binding partner and said second binding partner are specific for different analytes**; and

2) Fails to disclose a device where the first binding partner and the second binding partner **are located in different regions of said channel.**

Moreover, as explained above, because the Anderson *et al.* device comprises only a single binding partner (poly-T oligo) the device does not permit the detection of two or more target analytes. Consequently Anderson *et al.* fails to disclose a device or a method incorporating all the limitations of the presently claimed method. Accordingly, Anderson *et al.* fails to anticipate presently pending independent claim 1 or dependent claims 3-8, and 10-18 and the rejection of these claims under 35 U.S.C. §102(b) should be withdrawn.

If the Examiener wishes to maintain this rejection, Applicants request that she specifically identify **all of the elements of claim 1** in the reference. In particular, Applicants request that she identify **a first binding partner specific for a first analyte and a second binding partner specific for a second analyte, where the first binding partner and the second binding partner are specific for different analytes**, and where the first binding partner and the second binding partner are **are located in different regions of a channel.**

35 U.S.C. §103(a).

Claims 2, and 19-21 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Anderson *et al.* (U.S. Patent No: 6,168,948). Claim 9 was rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Anderson *et al. supra,* in view of Yager (U.S. Patent No: 6,007,775). The Examiner alleged that Anderson *et al.*, at col. 41, lines 31-58, teaches a method of detecting two or more analytes in a sample using a channel having affixed therein a binding partner for each of the two or more analytes where the binding partners are located in different regions of the channel. The Examiner further alleges that the recitation at col. 11, lines 20-21, that the analytes are "generally be labeled" suggests that the analytes are sometimes not labeled and argues that it would be obvious to sue the unlabeled analytes in the method of Anderson *et al.* With respect to claim 21, the Examiner argues it would be obvious using routine experimentation to amplify the analytes whereby analytes having an original concentration of less than 10-9 are detected. With respect to claim 9, the Examiner cites Yager as allegedly teaching the use of low Reynold's number channels. Applicants traverse.

A *prima facie* case of obviousness requires that the combination of the cited art, taken with general knowledge in the field, must provide all of the elements of the claimed invention. When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Geiger*, 815 2 USPQ2d 1276, 1278 (Fed. Cir. 1987).

Moreover, to support an obviousness rejection, the cited references must additionally provide a reasonable expectation of success. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), *citing In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

The combination of the cited references fails to teach or suggest the presently claimed invention. As explained above, the presently claimed methods involve:

> i) providing a channel having affixed therein **a first binding partner specific for a first analyte and a second binding partner specific for a second analyte, wherein said first binding partner and said second binding partner are specific for different analytes**, and **said first binding partner and said second binding partner are located in different regions of said channel** and said channel has a cross-sectional area small enough such that when analytes are released from said first binding partner and said second binding partner into a fluid flowing through said channel, said analytes remain spatially segregated until they reach a detection point in said channel downstream from said binding partners; [emphasis added] (claim 1)

Anderson *et al.* at most teaches the use of a reaction chamber **2910** comprising a single binding partner **2912** (poly-T oligos). This reference fails to teach the detection of multiple analytes or to teach or suggest a device comprising a channel having two or more binding partners. Accordingly, Anderson *et al.* fails to render the pending claims obvious.

The defects of Anderson *et al.* are not remedied by Yager. Yager describes a microfabricated sensor that produces a sample stream and a carrier stream that flow in layers, one on top of the other. Reagents (indicator molecules) are introduced into the carrier stream while a sample is introduced into the sample stream. As the reagents and sample diffuse together they produce a detectable signal.

The reagent and the sample interact in a fluid phase. Neither reagent nor sample are immobilized. The sensors described by Yager thus **do not** utilize a ". . . channel having affixed therein **a first binding partner specific for a first analyte and a second binding partner specific for a second analyte**. . . ". Indeed, the Examiner only cites Yager as allegedly teaching a channel having a Reynolds number below about 1.

Yager thus fails to remedy the deficiencies of Anderson *et al.*, and the combination of these references fails to provide the presently claimed invention. Accordingly, the Examiner has failed

to make her *prima facie* case, and the rejection of claims 2, and 19-21 under 35 U.S.C. §103(a) should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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Respectfully submitted,

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